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Limited Posterior Left Atrial Cryoablation in Patients With Chronic Atrial Fibrillation Undergoing Valvular Heart Surgery

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OBJECTIVES We sought to evaluate whether a limited surgical cryoablation of the posterior region of the left atrium was safe and effective in the cure of atrial fibrillation (AF) in patients with associated valvular heart disease.

BACKGROUND Extensive surgical ablation of AF is a complex and risky procedure. The posterior region of the left atrium seems to be important in the initiation and maintenance of AF.

METHODS In 32 patients with chronic AF who underwent heart valve surgery, linear cryolesions connecting the four pulmonary veins and the posterior mitral annulus were performed. Eighteen patients with AF who underwent valvular surgery but refused cryoablation were considered as the control group.

RESULTS Sinus rhythm (SR) was restored in 25 (78%) of 32 patients immediately after the operation. The cryoablation procedure required 20 ± 4 min. There were no intraoperative and perioperative complications. During the hospital period, one patient died of septicemia. Thirty-one patients reached a minimum of nine months of follow-up. Two deaths occurred but were unrelated to the procedure. Twenty (69%) of 29 patients remained in SR with cryoablation alone, and 26 (90%) of 29 patients with cryoablation, drugs and radiofrequency ablation. Three (10%) of 29 patients remained in chronic AF. Right and left atrial contractility was evident in 24 (92%) of 26 patients in SR. In control group, two deaths occurred, and SR was present in only four (25%) of 16 patients.

CONCLUSIONS Linear cryoablation with lesions connecting the four pulmonary veins and the mitral annulus is effective in restoration and maintenance of SR in patients with heart valve disease and chronic AF. Limited left atrial cryoablation may represent a valid alternative to the maze procedure, reducing myocardial ischemic time and risk of bleeding. (J Am Coll Cardiol 2000; 36:159–66) © 2000 by the American College of Cardiology

Atrial fibrillation (AF) is the most frequent supraventricular arrhythmia, and its pharmacologic therapy is not always satisfactory. However, it has been shown that a radical cure of AF might be possible. Cox et al. (1–4) were the first investigators who successfully treated AF using the maze procedure, which consisted of an extensive dissection with compartmentalization of both atria. Although effective, this long operation is rather complex and causes severe damage to the atria. Therefore, this procedure is not routinely used to cure AF in patients undergoing cardiovasculary surgery.

Recently, a catheter ablation technique mimicking the maze procedure has been proposed. Despite a relatively high success rate, it has a significant risk of complications (5–7). Moreover, catheter ablation of atrial foci localized in the pulmonary veins, which trigger AF, has been shown to be effective (8), but it is still limited to those patients with paroxysmal AF.

The possibility of performing selective ablation has several advantages, such as less atrial damage and, consequently, better preserved atrial mechanical function, shorter procedure time and less risk of related complications.

Previous studies in animals (9,10) and humans (11) have shown that ablation of limited atrial areas may be effective in the cure of AF. Few data available on left atrial mapping showed that the posterior wall seems to be a critical area for the maintenance of AF in patients with valvular heart disease (12). On the basis of these considerations, we decided to evaluate the effectiveness of linear cryoablation confined only to the posterior region of the left atrium between the pulmonary veins and the mitral annulus.

Cryoablation has been successfully used for over two decades in the surgical treatment of cardiac arrhythmias. It has been shown that cryoablation creates more homogeneous lesions and, above all, leaves the atrial endocardium intact (7,13). This may be important, especially in the future endeavors to reproduce such lesions with a transvenous catheter approach, because it could significantly reduce the risk of thromboembolism, which, at present, is the worst complication related to the extensive endocardial damage created by multiple radiofrequency (RF) deliveries.

Therefore, the objective of this study was to evaluate whether a limited surgical cryoablation of the posterior

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Abbreviations and Acronyms
AF = atrial fibrillation
ECG = electrocardiogram or electrocardiographic
RF = radiofrequency
SR = sinus rhythm

region of the left atrium was safe and effective in the cure of chronic AF in patients who also had valvular heart disease.

METHODS

Study group. The study group included 32 patients with chronic AF undergoing heart valve surgery owing to mitral or aortic valve disease, or both. Written, informed consent was required from all patients before the operation. Table 1 shows the patients' clinical characteristics in detail. The mean duration of AF was 6.1 ± 5.2 years. In 9% of patients, previous systemic embolization was reported. In the majority of patients, the mitral valve was diseased, only 6% being purely aortic. A cardiac reintervention was performed in 16% of patients.

Eighteen consecutive patients with chronic AF who were matched for age, AF duration and heart valve disease treated with valve surgery, but who refused the cryoablation procedure, were selected and considered as the control group.

Surgical procedure and cryoablation. All operations were performed by the same surgeon, under routine cardiopulmonary bypass with double venous cannulation and moderate hypothermia. The left atrium was opened through the usual left paraseptal incision after cold cardioplegic arrest. The left appendage, when present, was externally ligated at this moment. Once inspection of the mitral and/or aortic valves had been completed and the valve was repaired or removed, cryoablation was started.

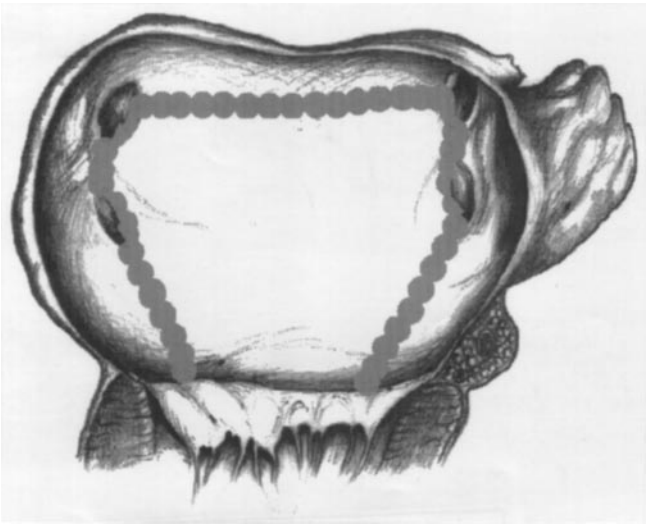

Figure 1. Schema of the procedure. The four pulmonary veins were isolated and the left atrial appendage was excised. The lesion lines connected the four pulmonary veins and the right and left lower pulmonary veins to the posterior mitral annulus.

A dual-probe cardiac cryosurgical system (Frigitronics, Cooper Surgical, Shelton, Connecticut) was used. The pressure in the two cylinders containing nitrous oxide (N_2O) was always maintained above 720 psi (pounds per square inch). The temperature fell abruptly to −60°C at the probe tip when gas was delivered and then maintained for 2 min. The two probes were used simultaneously, close to each other, to cut in half the duration and to not leave any gap between applications, as the acute endocardial lesion is not visible. Cryoablation was performed following the path counterclockwise (Fig. 1).

Finally, a mitral or aortic prosthesis was inserted, if required, and the operation continued as usual. At the end of extracorporeal circulation, adrenaline (0.025 gamma/kg

Table 1. Clinical Characteristics of Study Group

	Patients With Cryoablation (n = 32)	Patients Without Cryoablation (n = 18)	p Value
Gender (M/F)	14/18	3/15	NS
Age (years)	62 ± 10	68 ± 8	NS
NYHA class II	4 (13%)	3 (17%)	NS
NYHA class III	27 (84%)	14 (78%)	NS
NYHA class IV	1 (3%)	1 (5%)	NS
AF duration (years)	6.1 ± 5.2	6.9 ± 4.3	NS
LA diameter (mm)	52.5 ± 6.5	52.9 ± 6.2	NS
Underlying valve disease			
Mitral stenosis	9 (28%)	4 (22%)	NS
Mitral regurgitation	7 (23%)	2 (11%)	NS
Mitral stenosis and regurgitation	11 (34%)	4 (22%)	NS
Aortic stenosis	1 (3%)	2 (11%)	NS
Aortic stenosis and regurgitation	1 (3%)	2 (11%)	NS
Mitral plus aortic	3 (9%)	4 (22%)	NS
Previous embolic episodes	3 (9%)	2 (11%)	NS
Reoperation	5 (16%)	3 (17%)	NS

Data are presented as the number (%) of patients or mean value ± SD.
AF = atrial fibrillation; F = female; LA = left atrium; M = male; NS = not significant; NYHA = New York Heart Association functional class.

Table 2. Operation and Early Postoperative Data

	Patients With Cryoablation (n = 32)	Patients Without Cryoablation (n = 18)	p Value
Operation data			
MV replacement	20 (63%)	8 (45%)	NS
AV replacement	3 (9%)	4 (22%)	NS
MV plus AV replacement	1 (3%)	4 (22%)	NS
MV, plastic	8 (25%)	2 (11%)	NS
Bioprostheses	6 (19%)	2 (11%)	NS
Associate CABG	5 (16%)	1 (6%)	NS
ECC time (min)	84 ± 18	63 ± 21	0.001
ACC time (min	68 ± 17	48 ± 20	0.001
IABP	1 (3%)	0	NS
Rhythm outcome			
SR	25 (78%)	4 (22%)	< 0.001
AF	5 (16%)	14 (78%)	< 0.001
Junctional rhythm	2 (6%)	0	NS
Temporary pacemaker	12 (38%)	6 (33%)	NS
Early postoperative data			
Hospital stay (days)	7 ± 4	6 ± 2	NS
Direct current cardioversion	12 (37%)	17 (94%)	< 0.005
Revision bleeding	1 (3%)	0	NS
Revision valvular leak	1 (3%)	0	NS
Permanent pacemaker	1 (3%)	0	NS
Death	1 (3%)	1 (6%)	NS

Data are presented as the number (%) of patients or mean value ± SD.

ACC = aortic cross-clamp; AF = atrial fibrillation; AV = aortic valve; CABG = coronary artery bypass graft surgery; ECC = extracorporeal circulation; IABP = intra-aortic balloon pump; MV = mitral valve; NS = not significant; SR = sinus rhythm.

body weight per min) was administered to all patients. Intraoperative direct current cardioversion was routinely performed in all patients who had AF. Amiodarone infusion (150-mg loading dose over 10 to 15 min; then 1 mg/min for 6 h; then 0.5 mg/min until oral administration) was started after weaning from bypass, regardless of the heart rate or rhythm.

To assess whether the damage caused by exposure of the atrial endocardium to freezing was transparietal, an atrial biopsy was performed after cryoablation in eight patients at the beginning of our study.

Postoperative management and follow-up. During the hospital period, patients in both the AF/cryoablation and control groups were monitored by continuous electrocardiography. After intravenous infusion, oral amiodarone (600 mg/day for 10 days; then 400 mg/day for 10 days; then 200 mg/day) was administered to all patients, except for one in whom propafenone (300 mg twice a day) was preferred because of previous dysthyroidism. Antiarrhythmic therapy was routinely withdrawn after three months in the absence of AF recurrence. During the hospital stay, an attempt at electrical cardioversion was performed in all patients with AF.

After discharge, the patients were followed up with a clinical examination and electrocardiographic (ECG) and Holter monitoring at 1, 3, 6, 9, 12 and 18 months. In case symptoms recurred between follow-up visits, a clinical examination and ECG and Holter monitoring were performed and an event recorder was applied. Doppler echocardiography, with evaluation of transtricuspid and transmitral flow, was performed before discharge and at three and six months after the operation. After three months, oral anticoagulant therapy was discontinued in patients undergoing valvuloplasty who were in sinus rhythm (SR) with the presence of atrial contraction documented by Doppler echocardiography.

Statistical analysis. Continuous variables are expressed as the mean value ± SD. To compare outcomes, survival analysis and the log-rank test were used. Categoric variables were compared by using the chi-square test or the Fisher exact test, when appropriate. Results were considered to be statistically significant at $p < 0.05$. Statistical analysis was performed using the "Statistics" software (StatSoft Inc., Tulsa, Oklahoma).

RESULTS

Surgical procedure. Operative data are listed in Table 2. The mean aortic clamping time and extracorporeal circulation times were 20 and 21 min, respectively, longer than those times in the control group, reflecting the mean duration of the cryoablation procedure. Among patients with AF/cryoablation, a bioprosthesis was employed in six (19%) and valvuloplasty was performed in another eight (25%).

In the group of patients with AF/cryoablation, SR was restored in 25 patients (78%), either spontaneously or after intraoperative direct current cardioversion, immediately af-

Table 3. Follow-Up in Patients With Atrial Fibrillation Requiring Cryoablation and in the Control Group

	Hospital Discharge		1 Month		3 Months		6 Months		9 Months		12 Months	
	SR	AF	SR	AF	SR	AF	SR	AF	SR	AF	SR	AF
Cryo alone	—	—	—	—	21 (68%)	10 (32%)	21 (70%)	9 (70%)	20 (69%)	9 (31%)	15 (75%)	5 (25%)
Cryo + RFA	—	—	—	—	22 (71%)	9 (28%)	22 (73%)	8 (27%)	21 (73%)	8 (27%)	16 (80%)	4 (20%)
Cryo total	23 (74%)	8 (26%)	23 (74%)	8 (26%)	27 (87%)	4 (13%)	27 (90%)	3 (10%)	26 (90%)	3 (10%)	18 (90%)	2 (10%)
Control alone	—	—	—	—	2 (14%)	14 (86%)	2 (14%)	14 (86%)	2 (14%)	14 (86%)	2 (14%)	14 (86%)
Control total	2 (12%)	15 (88%)	4 (23%)	13 (77%)	4 (25%)	12 (75%)	4 (25%)	12 (75%)	4 (25%)	12 (75%)	4 (25%)	12 (75%)
	Alive	**Deaths**	**Alive**	**Deaths**	**Alive**	**Deaths**	**Alive**	**Deaths**	**Alive**	**Deaths**	**Alive**	**Deaths**
Cryoablation Group	31	0	31	0	31	0	30	1	29	2	20	3
Control Group	17	0	17	0	16	1	16	1	16	1	16	1

Data are presented as number (%) of patients.
AF = atrial fibrillation; cryo alone = patients with cryoablation alone; cryo + RFA = patients with cryoablation and radiofrequency ablation; cryo total = patients with cryoablation; radiofrequency ablation and antiarrhythmic drugs; control alone = control subjects with no antiarrhythmic drugs; control total = control subjects with and without antiarrhythmic drugs; SR = sinus rhythm.

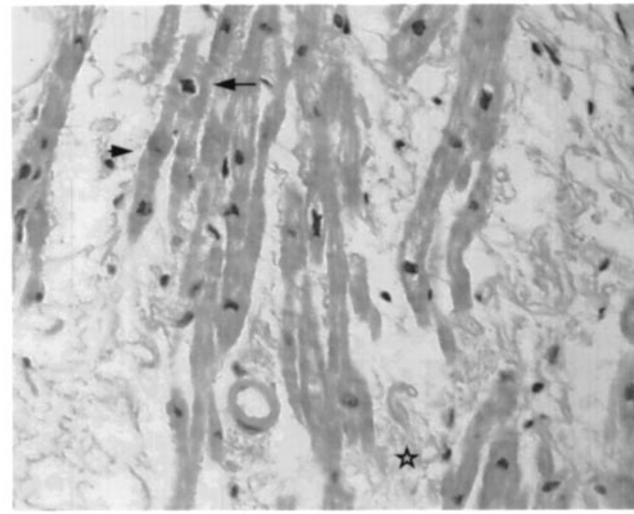

Figure 2. The photomicrograph shows nuclear changes **(arrow pointing left)**, irregular bands of contraction **(arrow pointing right)** and indistinct membranes **(star)** (Hematoxylin-eosin × 400)

ter the operation, as compared with four patients (22%) in the control group ($p < 0.001$). There were no intraoperative or perioperative complications. Inotropes were used in all patients in the immediate postoperative period both in the AF/cryoablation group and the control group. High doses of intravenous inotropes were used in three patients (9%) with postoperative low cardiac output syndrome in the AF/cryoablation group: one patient was in SR; the second one had AF; and the third one was in junctional rhythm. Also, in two patients in the control group, a high dose of intravenous inotropes were used. Both patients had AF. Atrial biopsies performed after cryoablation in eight patients revealed morphologic features indicating irreversible injury, such as nuclear and cytoplasmic degenerative lesions with no viable cardiomyocytes. The lesions involved the full thickness of the wall (Fig. 2).

Early postoperative period. Table 2 shows in detail the early postoperative data in patients with AF/cryoablation and in control subjects. The mean hospital stay was 7 ± 4 days (range 5 to 22) in patients with AF/cryoablation. There was no significant statistical difference in the hospital stay between patients with AF/cryoablation and control subjects. The number of direct current cardioversions performed was higher in the control group.

In the AF/cryoablation group, one patient (3%) had another operation within one week due to periprosthetic leakage. There was one in-hospital death (3%) because of septicemia occurring three weeks after the operation. This patient was in SR. In one patient (3%) with AF, a permanent pacemaker (VVI) was implanted because of symptomatic bradycardia.

Twenty-three (74%) of 31 patients with AF who underwent cryoablation were in SR at the time of hospital discharge.

In the control group, one patient died from heart failure the day after the operation. Among the remaining

17 patients, only two (12%) were in SR at the time of discharge, despite attempts at electrical cardioversion.

Follow-up. In the cryoablation group at three-month follow-up, 27 (87%) of 31 patients were in SR. Among these patients, 21 (68%) with treated with cryoablation only.

Four patients (13%) had a few episodes of paroxysmal AF during the first three months, but they maintained SR during the remaining follow-up period. All four patients received antiarrhythmic drugs: two received amiodarone and two received propafenone.

Two patients (6%) were in SR with episodes of paroxysmal atrial tachycardia. Both patients underwent an electrophysiologic study with a nonfluoroscopic mapping system (CARTO, Biosense-Webster). In one patient, the mapping revealed a pattern of radial activation modified by intervening scar tissue, resembling a pattern of perimitral reentry. A single application of RF energy at the site of earliest activation was effective in eliminating the tachycardia, suggesting a focal mechanism. In the second patient, the atrial mapping did not determine the tachycardia mechanism. Neither entrainment nor RF energy application between the right inferior pulmonary vein and the mitral annulus, where a gap was present, further clarified the nature of the atrial tachycardia. The patient underwent electrical cardioversion with restoration of normal SR, and sotalol therapy (80 mg twice a day) was initiated. No further episodes of atrial tachycardia or AF were detected in both patients.

All patients reached a minimum of nine months of follow-up, during which two deaths occurred. One patient with chronic AF died of heart failure four months after the operation, and the other one in SR died of intracerebral hemorrhage after seven months of follow-up. The patient was not taking anticoagulant agents because of a bioprosthesis.

Of the remaining 29 patients, 26 were in SR at nine months. Of these patients, 20 (69%) were in SR and had cryoablation alone; 21 (73%) had cryoablation and RF ablation; and 26 (90%) had cryoablation and RF ablation and took antiarrhythmic drugs (Fig. 3).

This trend was maintained at 12 months, at which time 18 (90%) of 20 patients remained in SR with cryoablation, RF ablation and antiarrhythmic drugs.

After the cryoablation procedure, 12 patients, including the aforementioned two patients with episodes of atrial tachycardia, underwent an electrophysiologic study, which did not show fibrillation in any part of the left atrium.

Table 3 shows the characteristics of cardiac rhythm in patients with AF/cryoablation at discharge and 1, 3, 6, 9 and 12 months.

In the control group at three-month follow-up, one death occurred from heart failure. In the remaining 16 patients, four (25%) were in SR: two who took an antiarrhythmic drug and two who did not. Two patients were discharged in SR that was maintained during follow-up. In two patients, electrical cardioversion was successful one month after the operation and no more episodes of AF were detected. The remaining 12 patients (75%) had chronic AF. This trend was consistent at 6, 9 and 12 months of follow-up (Fig. 3).

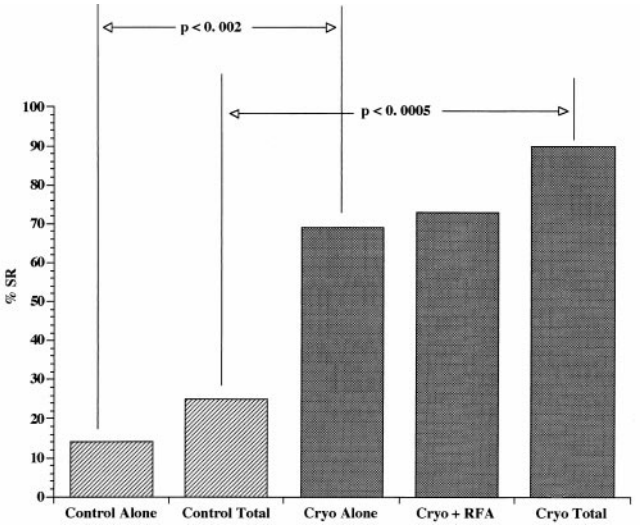

Figure 3. Follow-up results. Bar graph shows the number of patients in SR, expressed as percentage, in the AF/cryoablation group and in the control group at nine-month follow-up. Control alone = control subjects with no antiarrhythmic drugs; control total = control subjects with and without antiarrhythmic drugs; cryo alone = patients with cryoablation only; cryo + RFA = patients with cryoablation and RF ablation; cryo total = patients with cryoablation, RF ablation and antiarrhythmic drugs.

The difference in outcome between the two groups was statistically significant during follow-up ($p < 0.0001$) (Fig. 4).

When comparing patients in SR with those with AF after cryoablation, no statistically significant difference was seen regarding the patients' age, right and left atrial size, type of surgical procedure and duration of extracorporeal circulation and aortic clamping time. The difference in duration of AF was not statistically significant, but it was longer than 10 years in three of four patients who still had chronic AF at the end of follow-up (188, 144 and 132 months, respectively).

Among patients with AF who underwent cryoablation, one in SR had another operation for mitral valvuloplasty failure one month later; interestingly, during the second operation, no evidence of the cryoablation lesions was present on gross inspection of the endocardium. Another patient required implantation of a dual-chamber permanent pacemaker because of symptomatic sinus bradycardia four months after the initial procedure.

Doppler echocardiography revealed the presence of right and left atrial contractility in 24 (92%) of the 26 patients in SR.

DISCUSSION

Major findings. There were three major findings from this study: 1) The creation of a few linear cryolesions in the posterior region of the left atrium in patients with chronic AF undergoing heart valve surgery is effective in restoration

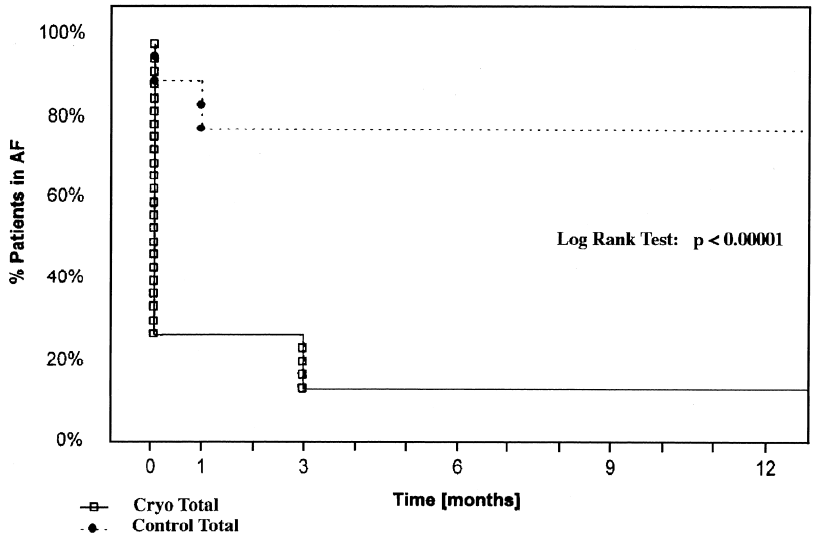

Figure 4. Difference in outcome between the AF/cryoablation group and the control group during follow-up. Cryo total = patients with cryoablation, RF ablation and antiarrhythmic drugs; control total = control subjects with and without antiarrhythmic drugs.

and maintenance of SR, allowing for the recovery of atrial function in the majority of the patients. 2) Our procedure has proved to be feasible and requires only a little extra time to the heart valve surgery time (~20 min). 3) The atrial linear lesions created by cryoablation during cardiac surgery have shown to be safe.

Electrophysiologic background. It is generally accepted that the electrophysiologic substrate responsible for the maintenance of AF is the presence of multiple, simultaneous reentrant waves circulating through the atrial tissue (14,15). The surgical maze procedure divides the atrial myocardium into multiple, small segments, thus reducing the mass of tissue electrically activated and impeding the multiple wavelets of reentry to be sustained.

However, several recent reports (9,11,16,17) have shown that different patterns of electrical activity in various atrial regions are present during AF, with the simultaneous presence of regions with relatively regular activation and other areas with completely disorganized atrial activity. These studies suggested that the fibrillatory process is far from random and seems to be significantly influenced by anatomic and electrophysiologic factors. Therefore, although the atria, as a whole, participate in the process of AF, not all the atrial regions contribute equally to the perpetuation of fibrillation. This hypothesis also seems to be corroborated by the success of selective ablation of critical areas reported in some cases (9,11). Many studies point to the importance of the posterior region of the left atrium as a critical area in the maintenance of AF, both in animals (9) and humans (6,8,12,18). Morillo et al. (9) showed that in dogs, the shortest FF intervals during AF were recorded in the left posterior wall. Cryoablation limited to this zone was effective in terminating and preventing reinduction of the arrhythmia in 82% of cases. Sueda et al. (12) showed that in patients with chronic AF and mitral valve disease, the areas with the shortest FF intervals were at the base of the left atrial appendage and the posterior wall lateral to the left pulmonary veins. Furthermore, they demonstrated that the surgical isolation of these areas restored SR in most patients. The importance of the left atrium in the maintenance of AF is also confirmed by reports on percutaneous catheter ablation of AF (5,6,8), showing a higher success rate when linear lesions were applied within the left atrium. However, the safety of a procedure that includes extensive ablation of the left atrium has not been sufficiently demonstrated, and severe complications, such as cardiac tamponade or thromboembolism, have been reported (5–7). This risk of severe complications encourages us to limit the ablation areas as much as possible. Identifying localized atrial regions responsible for the initiation and maintenance of AF would be crucial for a safe and effective ablation procedure.

Recently, Haissaguerre et al. (8) showed that in patients with idiopathic AF, the pulmonary veins represent important areas in triggering and maintaining AF, and RF ablation limited to these areas was successful in a high percentage of cases.

In our study, using cryoenergy, we performed linear lesions connecting the four pulmonary veins and the inferior pulmonary veins to the posterior mitral annulus with the purpose of isolating this area. Our results confirmed the critical role of the posterior region of the left atrium. It is still not possible to establish whether the restoration of SR depends on the modification of the substrate of AF by the linear lesions or whether it is due to the isolation or elimination of potential focal triggers within the pulmonary veins, or a combination of both mechanisms.

In contrast, we should consider that the creation of linear lesions, especially incomplete ones, may represent a substrate for the occurrence of new intra-atrial tachycardias whose mechanism is difficult to establish.

Comparison with previous studies. Over the last decade, several reports have presented different surgical techniques

to cure AF (1–4,12,18,19–21). The corridor operation was the first one to show that operation may control AF (19). It consists of isolating a strip of atrial tissue (corridor) that harbors the sinus node and the atrioventricular node. It was observed that the left atrium remained in AF, pointing to the importance of the left atrium in the genesis of AF. Graffigna et al. (21) have reported that 71% of patients with mitral valve disease returned to SR after left atrial isolation. With these surgical approaches the problem is the persistence of AF in the left atrium or part of it leaving the hemodynamic and thromboembolic problems unresolved. The maze procedure was shown to be effective in eliminating AF and restoring atrial contractility in the majority of patients (1–4). In a long-term follow-up study, the maze procedure had a success rate of 93% for restoration of SR, without use of antiarrhythmic drugs, in a population mostly characterized by idiopathic AF (3). Kosakai et al. (20) reported that the maze procedure was effective in maintaining SR also in patients with organic heart disease, even if ~30% of patients did not present with left atrial contraction during follow-up. However, the maze procedure is time-consuming and requires an intricate pattern of atrial incisions, extensive suturing, relevant blood loss and a prolonged cardiopulmonary bypass.

With the aim of minimizing blood loss and reducing the cardiopulmonary bypass time, Chen et al. (22) have simulated the classic maze operation in 12 patients undergoing mitral valve surgery by using the combination of RF catheter ablation and cryoablation instead of extensive atrial surgical incisions. They reported that at the end of six-month follow-up, SR was restored in 60% of patients, but only 30% of patients showed left atrial contractility. Recently, Sueda et al. (12,18) developed a surgical procedure mainly involving the posterior wall of the left atrium for treatment of chronic AF associated with mitral valve disease. They reported a disappearance of AF at six months after the operation in 78% of patients, with recovery of left atrial contractility in 61% of patients.

In our study, we chose to limit the part of the left atrium involved in the procedure as much as possible to reduce the time of the operation and to preserve normal atrial contractility, and we used only cryoenergy to perform the linear lesions. During follow-up, we observed restoration of SR in 90% of the patients. In 69% of patients, cryoablation alone was sufficient to maintain normal SR; one patient also required RF ablation of atrial tachycardia; and five patients also had pharmacologic therapy. The early success of the cryoablation procedure is predictive of long-term efficacy. The proarrhythmic effect related to the cryoablation scar, although present, appears to be minimal, and in some cases can be resolved with RF ablation. We have not found variables predictive of failure, but we noticed that in patients who still had chronic AF after the cryoablation procedure, a long AF duration (>10 years) was evident in three of four patients. Most important, the majority of the patients (92%) in SR showed restored right and left atrial contractility. Furthermore, the procedure required only 20 min, and the aortic cross-clamp time and cardiopulmonary bypass times were very short in comparison with those in previous studies (1,4,18,20,22). This significant reduction of myocardial ischemic time may allow us to perform this procedure routinely in patients with AF undergoing heart valve surgery.

Potential advantages of cryoablation. The risk of thromboembolic complications in patients undergoing multiple linear lesions in the left atrium using RF energy is high (5,7). We chose to deploy cryothermy as an alternative energy source to create linear lesions for two reasons. First, cryoablation has the advantage of leaving the endocardium intact (7,13,23), thus reducing the thromboembolic risk, as demonstrated by most of the data on surgical cryoablation (7,24,25) as well as by experimental studies (13,23,26,27). Second, the lesion created by cryoablation has been demonstrated to be transmural and well circumscribed. The chronic scar is made of dense fibrotic tissue without viable cardiomyocytes, with no tendency to rupture or dilate, because cryoablation induces necrosis of myocardial tissue but spares the collagenous fiber (13,25–27), as confirmed by our histologic data. In contrast, the lesions produced with RF energy are less circumscribed and nonhomogeneous, with clear evidence of viable cardiomyocytes, and, most important, this energy causes endocardial disruption with a consequent potential risk of a thromboembolic event (13).

Clinical implications. The study shows that cryoablation, creating linear lesions connecting the four pulmonary veins and the inferior pulmonary veins to the mitral annulus in patients with chronic AF and valvular heart disease, is effective. Moreover, the procedure is simpler and faster, with less atrial damage, than the maze operation.

These data are important if we consider that elimination of AF and maintenance of atrial contractility provide hemodynamic benefit, especially in patients with associated heart disease; moreover, the use of anticoagulant therapy may be avoided in those patients who undergo valvuloplasty or a bioprosthesis operation.

Furthermore, these data may also be used for the reproduction of the same type of lesions using percutaneous catheter ablation in patients with chronic AF with or without associated heart disease, avoiding the need of open heart surgery and related complications.

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REFERENCES

1. Cox JL, Schessler RB, D'Agostino HJ, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure. J Thorac Cardiovasc Surg 1991;101:569–92.
2. Cox JL, Boineau JP, Schuessler RB, Kater KM, Lappas DG. Five year experience with the maze procedure for atrial fibrillation. Ann Thorac Surg 1993;56:814–24.
3. Cox JL, Schuessler RB, Lappas DG, Boineau JP. An 8-1/2 year experience with surgery for atrial fibrillation. Ann Surg 1996;224:267–73.
4. Cox JL, Jaquiss RDB, Schuessler RB, Boineau JP. Modification of the maze procedure for atrial flutter and atrial fibrillation. II. Surgical technique of the maze III procedure. J Thorac Cardiovasc Surg 1995;110:485–95.
5. Maloney JD, Milner L, Barold S, Czerska B, Markel M. Two-staged biatrial linear and focal ablation to restore sinus rhythm in patients with refractory chronic atrial fibrillation: procedure experience and follow-up beyond 1 year. Pacing Clin Electrophysiol 1998;21:2527–32.
6. Haissaguerre M, Jais P, Shah DC, et al. Right and left atrial radiofrequency catheter therapy of paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol 1996;7:1132–44.
7. Zhou L, Keane D, Reed G, Ruskin J. Thromboembolic complications of cardiac radiofrequency catheter ablation: a review of the reported incidence, pathogenesis and current research directions. J Cardiovasc Electrophysiol 1999;10:611–20.
8. Haissaguerre M, Jais P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998;339:659–66.
9. Morillo CA, Klein GJ, Jones DL, Guiraudon CM. Chronic rapid atrial pacing: structural, functional, and electrophysiological characteristics of a new model of sustained atrial fibrillation. Circulation 1995;91:1588–95.
10. Li H, Hare J, Mughal K, et al. Distribution of atrial electrogram types during atrial fibrillation: effect of rapid atrial pacing and intercaval junction ablation. J Am Coll Cardiol 1996;27:1713–21.
11. Gaita F, Riccardi R, Calò L, et al. Atrial mapping and radiofrequency catheter ablation in patients with idiopathic atrial fibrillation: electrophysiologic findings and ablation results. Circulation 1998;97:2136–45.
12. Sueda T, Nagata H, Shikata H, et al. Simple left atrial procedure for chronic atrial fibrillation associated with mitral valve disease. Ann Thorac Surg 1996;62:1796–800.
13. Rodriguez LM, Leunissen J, Hoekstra A, et al. Transvenous cold mapping and cryoablation of the AV node in dogs: observations of chronic lesions and comparison to those obtained using radiofrequency ablation. J Cardiovasc Electrophysiol 1998;9:1055–61.
14. Moe G. On the multiple wavelet hypothesis of atrial fibrillation. Arch Int Pharmacodyn Ther 1962;140:183–8.
15. Konings KTS, Kirchhof CJHJ, Smeets JRLM, Wellens HJJ, Penn OC, Allessie MA. High-density mapping of electrically induced atrial fibrillation in humans. Circulation 1994;89:1665–80.
16. Konings KTS, Smeets JLRM, Penn OC, Wellens HJJ, Allessie MA. Configuration of unipolar atrial electrograms during electrical induced atrial fibrillation in humans. Circulation 1997;95:1231–41.
17. Kumagai K, Khrestian C, Waldo AL. Simultaneous multisite mapping studies during induced atrial fibrillation in the sterile pericarditis model: insight into the mechanism of its maintenance. Circulation 1997;95:511–21.
18. Sueda T, Nagata H, Orihashi K. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. Ann Thorac Surg 1997;63:1070–5.
19. Leitch JW, Klein GJ, Yee R, Guiraudon GM. Sinus node atrioventricular node isolation: long-term results with the "corridor" operation for atrial fibrillation. J Am Coll Cardiol 1991;17:970–5.
20. Kosakai Y, Kawaguchi A, Isobe F, et al. Modified maze procedure for patients with atrial fibrillation undergoing simultaneous open heart surgery. Circulation 1995;92 Suppl II:II-359–64.
21. Graffigna A, Pagani F, Minzioni G, Salerno J, Viganò M. Left atrial isolation associated with mitral valve operations. Ann Thorac Surg 1992;54:1093–8.
22. Chen MC, Guo BF, Chang JP, Yeh KH, Fu M. Radiofrequency and cryoablation of atrial fibrillation in patients undergoing valvular operations. Ann Thorac Surg 1998;65:1666–72.
23. Keane D, Zhou L, Houghtaling C, et al. Percutaneous cryothermal catheter ablation for the creation of linear atrial lesions (abstr). Pacing Clin Electrophysiol 1999;22:847.
24. Gallagher JJ, Sealy WC, Anderson RW, et al. Cryosurgical ablation of accessory atrioventricular connection: a method for correction of the preexcitation syndrome. Circulation 1977;55:471–9.
25. Avitall B, Gupta G, Millard S, Helms R. Catheter designs for interventional electrophysiology. In: Singer I, editor. Nonpharmacological Therapy of Arrhythmias for the 21st Century: The State of the Art. Armonk (NY): Futura, 1998:291–335.
26. Klein GJ, Harrison L, Ideker RF, et al. Reaction of the myocardium to cryosurgery: electrophysiology and arrhythmogenic potential. Circulation 1979;59:364–8.
27. Fujino H, Thompson RP, Germroth PG, Harold ME, Swindle M, Gillette PC. Histologic study of chronic catheter cryoablation of atrioventricular conduction in swine. Am Heart J 1993;125:1632–7.